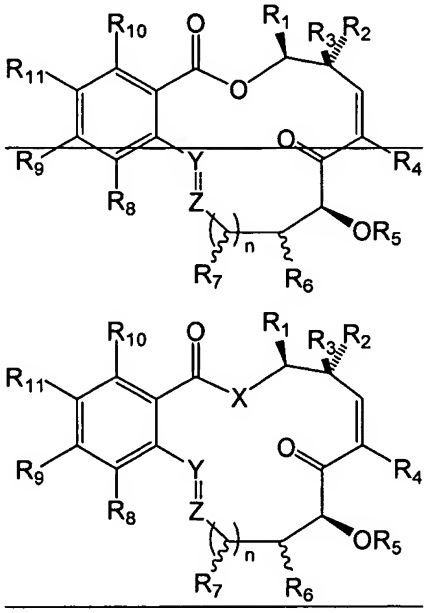
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. **(Currently Amended)** A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or pharmaceutically acceptable derivative thereof;

wherein $\mathbf{R_1}$ is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;

$\mathbf{R_2}$ ~~and~~ is methyl;

$\mathbf{R_3}$ ~~are each independently~~ is hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or

~~R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or~~

R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;

$\mathbf{R_4}$ is hydrogen or halogen;

$\mathbf{R_5}$ is ~~hydrogen, an oxygen protecting group or a prodrug~~ hydrogen or an oxygen protecting group;

$\mathbf{R_6}$ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

$\mathbf{R_7}$, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

$\mathbf{R_8}$ is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

$\mathbf{R_9}$ is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $-X_1(CH_2)_pX_2-R_{14}$, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $-(C=O)NHR_{15}$ $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an aliphatic moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

$\mathbf{R_{10}}$ is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

$\mathbf{R_{11}}$ is hydrogen, hydroxyl or protected hydroxyl;

X is O, NH or CH_2;

Y is CHR_{17}, O, CR_{17} or NR_{17}; and **Z** is CHR_{18}, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken together

is –O-, -CH_2- or -NR_{19}-, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond;

wherein the compound is present in an amount effective to inhibit production of a pro-inflammatory and/or immunologic cytokine.

2. **(Currently Amended)** The composition of claim 1, wherein:

R_1 is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R_2 ~~and~~ is methyl;

R_3 ~~are each independently~~ is hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

~~R_1 and R_2, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen; or~~

R_1 and R_3, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R_4 is hydrogen or halogen;

R_5 is hydrogen or a protecting group;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or lower alkyl optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;

R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, -$X_1(CH_2)_pX_2$-R_{14}, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -$X_1(CH_2)_pX_2$-R_{14};

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, lower alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or a protecting group, or R_{12} and R_{13},

taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is –(C=O)NHR_{15} –(C=O)OR_{15}, or –(C=O)R_{15}, wherein each occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or R_{14} is $–SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

$\mathbf{R_{10}}$ is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

$\mathbf{R_{11}}$ is hydrogen, hydroxyl or protected hydroxyl;

X is O;

Y is CHR_{17}, CR_{17} or NR_{17}; and **Z** is CHR_{18}, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or lower alkyl, or R_{17} and R_{18} taken together is –O-, $-CH_2-$ or $-NR_{19}-$, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond.

3. **(Previously Presented)** The composition of claim 2, where n is 1.

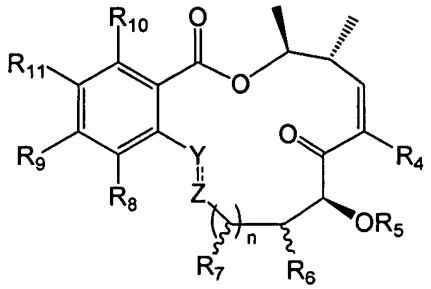
4. **(Original)** The composition of claim 2, where R_4 is halogen.

5. **(Original)** The composition of claim 2, where R_4 is fluorine.

6. **(Original)** The composition of claim 2, where Y and Z together represent-CH=CH-

7. **(Original)** The composition of claim 2, where Y and Z together represent trans –CH=CH-.

8. **(Previously Presented)** The composition of claim 2, wherein R_1 and R_2 are each methyl and R_3 is hydrogen and the compound has the structure:



wherein R_4-R_{11}, n, Y and Z are as defined in claim 2.

9. **(Previously Presented)** The composition of claim 8, wherein n is 1.

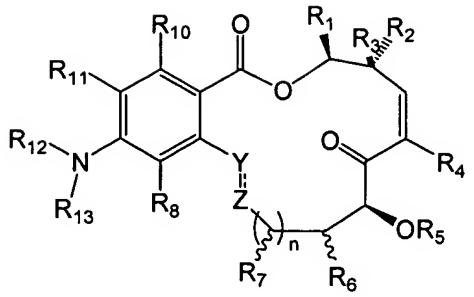
10. **(Original)** The composition of claim 8, wherein R_4 is halogen.

11. **(Original)** The composition of claim 8, wherein Y and Z together represent –CH=CH.

12. **(Previously Presented)** The composition of claim 8, wherein n is 1, R_4 is halogen and Y and Z together represent –CH=CH-.

13. **(Original)** The composition of claim 11 or 12 wherein –CH=CH- is *trans*.

14. **(Previously Presented)** The composition of claim 2, wherein R_9 is $NR_{12}R_{13}$ and the compound has the structure:



wherein R_1-R_{13}, n, Y and Z are as defined in claim 2, or

R_{13} and R_8 may, when taken together, form a cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydrogen, alkyloxy, amino, alkylamino, aminoalkyl, and halogen.

15. **(Previously Presented)** The composition of claim 14, wherein n is 1.

16. **(Original)** The composition of claim 14, wherein R_4 is halogen.

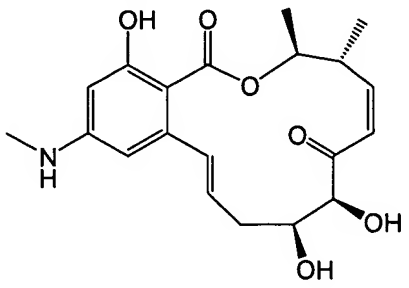
17. **(Original)** The composition of claim 14, wherein Y and Z together represent –CH=CH-.

18. **(Original)** The composition of claim 14, wherein R_1 and R_2 are each methyl and R_3 is hydrogen.

19. **(Previously Presented)** The composition of claim 14, wherein n is 1, R_1 and R_2 are each methyl, R_3 is hydrogen, R_4 is halogen, and Y and Z together represent –CH=CH-.

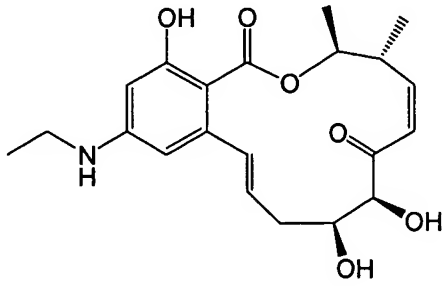
20. **(Original)** The composition of claim 17 or 19, wherein –CH=CH- is trans.

21. **(Original)** The composition of claim 1 wherein the compound has the structure:



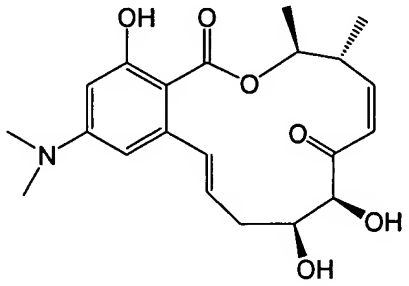
or pharmaceutically acceptable derivative thereof.

22. **(Original)** The composition of claim 1 wherein the compound has the structure:



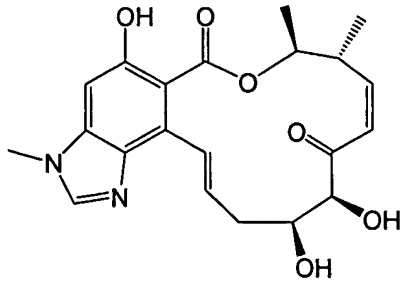
or pharmaceutically acceptable derivative thereof.

23. **(Original)** The composition of claim 1 wherein the compound has the structure:



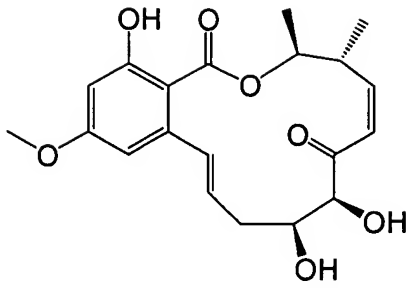
or pharmaceutically acceptable derivative thereof.

24. **(Original)** The composition of claim 1 wherein the compound has the structure:



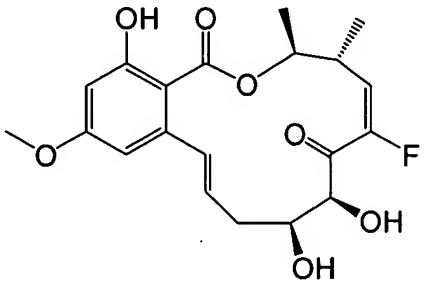
or pharmaceutically acceptable derivative thereof.

25. **(Original)** The composition of claim 1 wherein the compound has the structure:



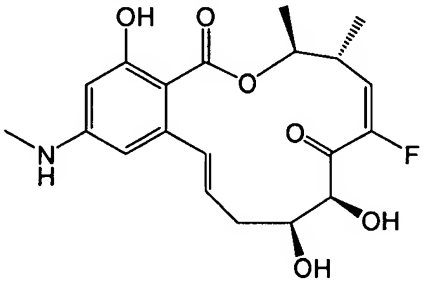
or pharmaceutically acceptable derivative thereof.

26. **(Original)** The composition of claim 1 wherein the compound has the structure:



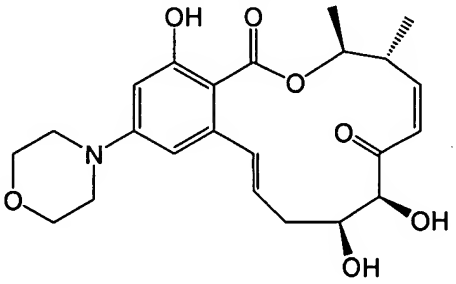
or pharmaceutically acceptable derivative thereof.

27. **(Original)** The composition of claim 1 wherein the compound has the structure:



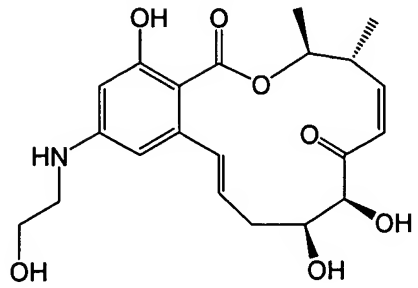
or pharmaceutically acceptable derivative thereof.

28. **(Original)** The composition of claim 1 wherein the compound has the structure:



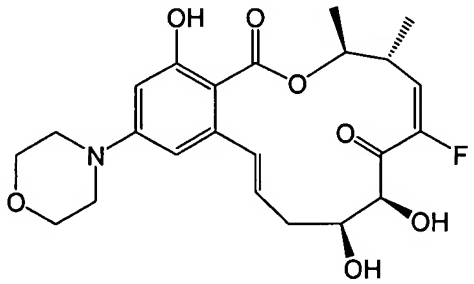
or pharmaceutically acceptable derivative thereof.

29. **(Original)** The composition of claim 1 wherein the compound has the structure:



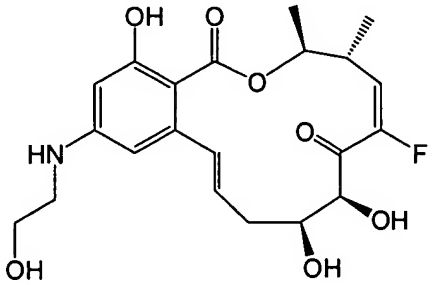
or pharmaceutically acceptable derivative thereof.

30. **(Original)** The composition of claim 1 wherein the compound has the structure:



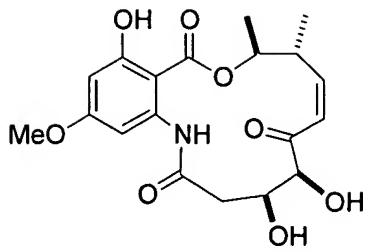
or pharmaceutically acceptable derivative thereof.

31. **(Original)** The composition of claim 1 wherein the compound has the structure:



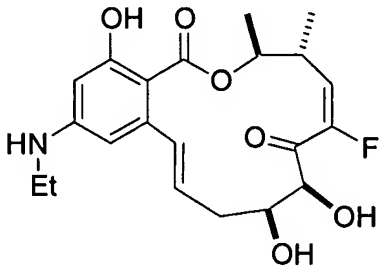
or pharmaceutically acceptable derivative thereof.

32. **(Original)** The composition of claim 1 wherein the compound has the structure:



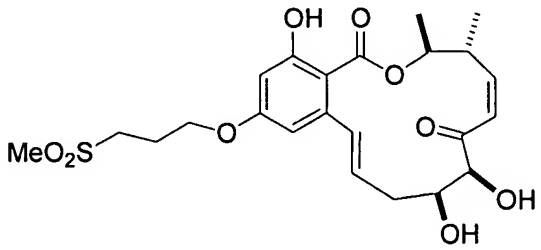
or pharmaceutically acceptable derivative thereof.

33. **(Original)** The composition of claim 1 wherein the compound has the structure:



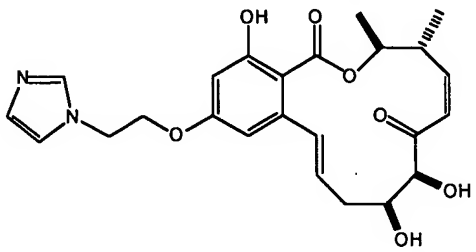
or pharmaceutically acceptable derivative thereof.

34. **(Original)** The composition of claim 1 wherein the compound has the structure:



or pharmaceutically acceptable derivative thereof.

35. **(Original)** The composition of claim 1 wherein the compound has the structure:



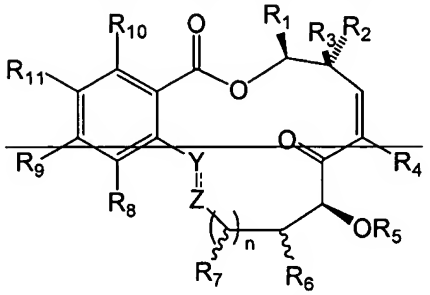
or pharmaceutically acceptable derivative thereof.

36. **(Original)** The pharmaceutical composition of claim 1, wherein the composition is for oral administration.

37. **(Canceled)**

38. **(Previously Presented)** The pharmaceutical composition of claim 1, wherein the pro-inflammatory and/or immunologic cytokine is TNFα, IL-1, IL-6, IL-8 or IL-2.

39. **(Currently Amended)** A method for treating rheumatoid arthritis, psoriasis, asthma, sepsis, inflammatory bowel disease, atopic dermatitis or Crohn's disease comprising the step of systemically administering to a subject in need thereof ~~a pharmaceutically suitable carrier or diluent and a therapeutically effective amount of a compound having the structure:~~ a therapeutically effective amount of a pharmaceutical composition of claim 1.



~~or pharmaceutically acceptable derivative thereof;~~

~~wherein R_1 is hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl;~~

~~R_2 and R_3 are each independently hydrogen, halogen, hydroxyl, protected hydroxyl, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or~~

~~R_1 and R_2, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms; or~~

~~R_1 and R_3, when taken together, may form a substituted or unsubstituted, saturated or unsaturated cyclic ring of 3 to 8 carbon atoms;~~

~~R_4 is hydrogen or halogen;~~

~~R_5 is hydrogen, an oxygen protecting group or a prodrug;~~

~~R_6 is hydrogen, hydroxyl, or protected hydroxyl;~~

~~n is 0-2;~~

~~R_7, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;~~

~~R_8 is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or an aliphatic moiety optionally substituted with hydroxyl, protected hydroxyl, SR_{12}, or $NR_{12}R_{13}$;~~

~~R_9 is hydrogen, halogen, hydroxyl, protected hydroxyl, OR_{12}, SR_{12}, $NR_{12}R_{13}$, $X_1(CH_2)_pX_2$-R_{14}, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or $X_1(CH_2)_pX_2$-R_{14};~~

~~wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or a protecting group, or R_{12} and R_{13}, taken together may form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,~~

~~wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or N(alkyl), or wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,~~

~~p is 2-10, and~~

~~R_{14} is hydrogen, or an aryl, heteroaryl, alkylaryl, or alkylheteroaryl moiety, or is $(C=O)NHR_{15}$, $(C=O)OR_{15}$, or $(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl; or R_{14} is $SO_2(R_{16})$, wherein R_{16} is an aliphatic moiety, wherein one or more of R_{14}, R_{15}, or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or~~

~~R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;~~

~~R_{10} is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;~~

~~R_{11} is hydrogen, hydroxyl or protected hydroxyl;~~

~~Y is CHR_{17}, CR_{17} or NR_{17}; and Z is CHR_{18}, C=O, CR_{18} or NR_{18}, wherein each occurrence of R_{17} and R_{18} is independently hydrogen or aliphatic, or R_{17} and R_{18} taken together~~

~~is O, CH_2 or NR_{19}, wherein R_{19} is hydrogen or lower alkyl, and Y and Z may be connected by a single or double bond;~~

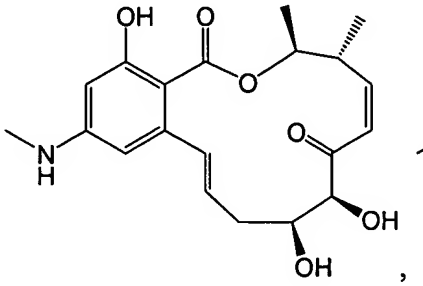
~~wherein the compound is present in an amount effective to inhibit production of a pro-inflammatory and/or immunologic cytokine~~.

40. **(Original)** The method of claim 39, wherein the compound is administered orally.

41. **(Canceled)**

42. **(Previously Presented)** The method of claim 39, wherein the method is for treating psoriasis.

43. **(Currently Amended)** The method of claim 41, wherein the compound has any one of the following structures:



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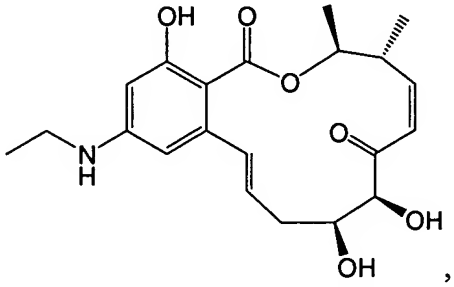

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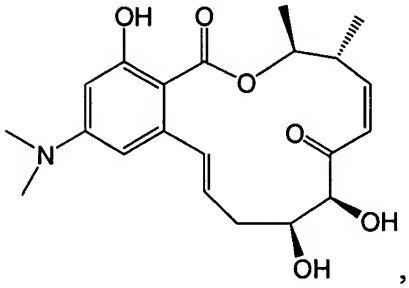

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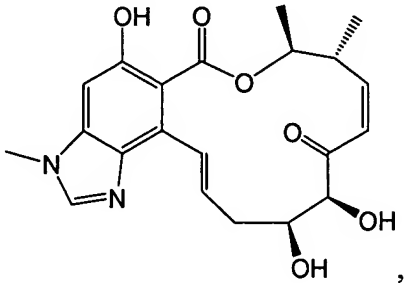

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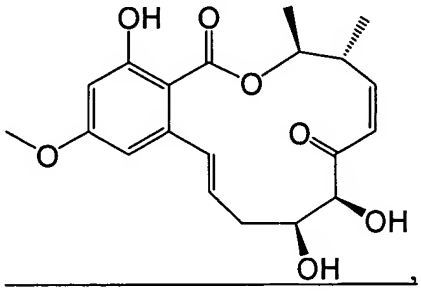

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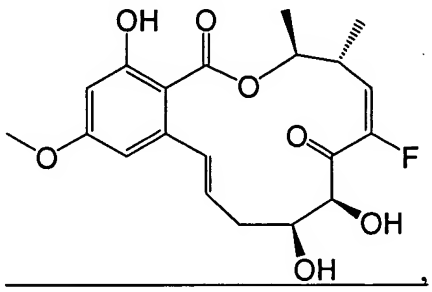

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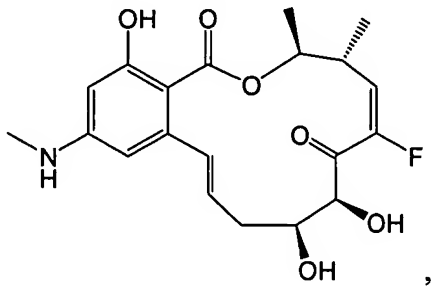

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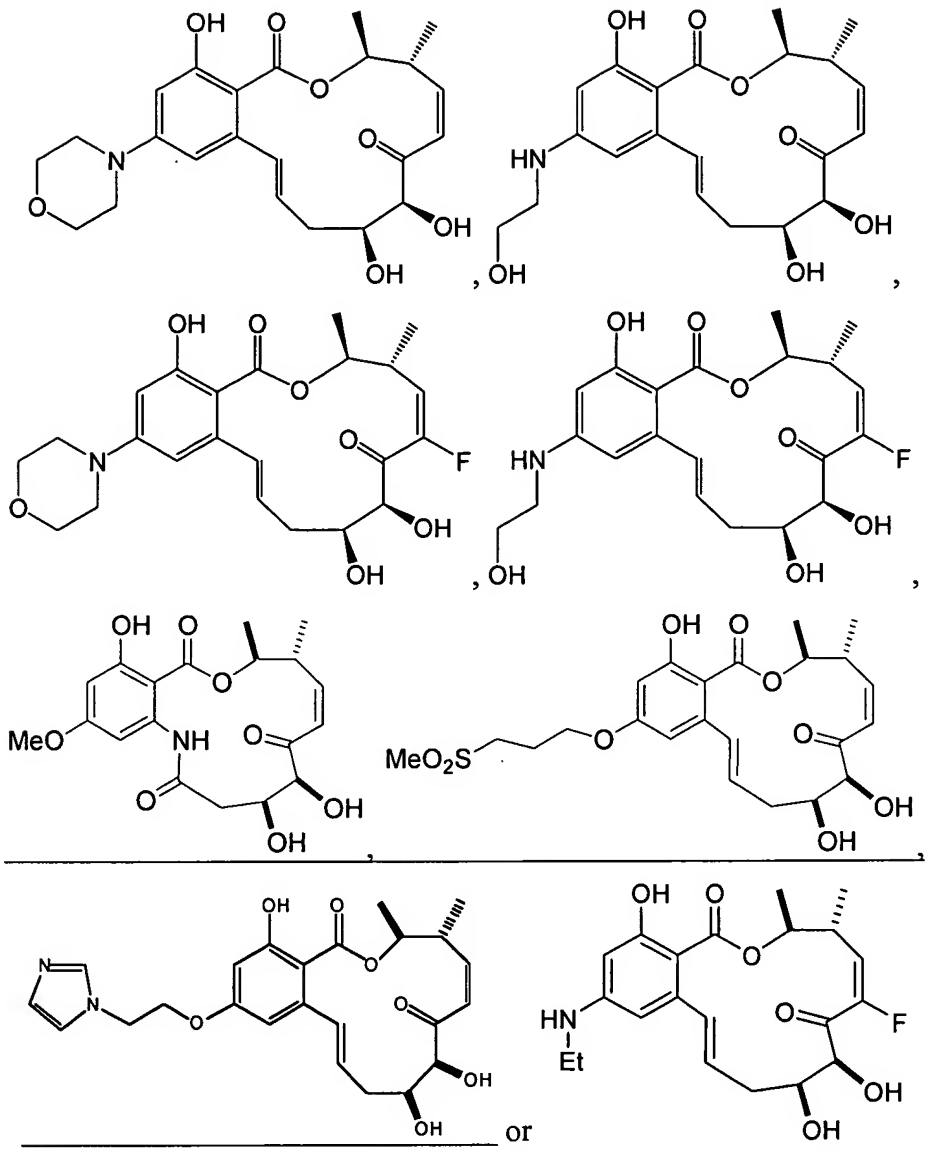


or pharmaceutically acceptable derivative thereof.

44. **(Canceled)**

45. **(Previously Presented)** The method of claim 39, wherein the pro-inflammatory and/or immunologic cytokine is TNFα, IL-1, IL-6, IL-8 or IL-2.

46. **(New)** The composition of claim 2, where R_1 is hydrogen or methyl.

47. **(New)** The composition of claim 2, where R_3 is hydrogen or halogen.

48. **(New)** The composition of claim 2, where R_4 is hydrogen.

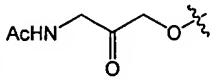
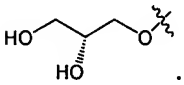
49. **(New)** The composition of claim 2, where R_5 is hydrogen.

50. **(New)** The composition of claim 2, where R_6 is hydroxyl.

51. **(New)** The composition of claim 2, where R_7 is hydrogen or hydroxyl.

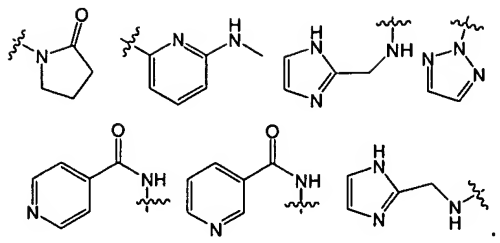
52. **(New)** The composition of claim 2, where R_8 is hydrogen or halogen.

53. **(New)** The composition of claim 2, where R_9 is hydroxyl, protected hydroxyl, $-OR_{12}$, $-NR_{12}R_{13}$ or $-O(CH_2)_pX_2R_{14}$, wherein R_{12}, R_{13}, R_{14} and X_2 are as defined in claim 2.

54. **(New)** The composition of claim 53, where R_9 is $-OR_{12}$, wherein R_{12} is methyl, ethyl, propyl, isopropyl, butyl, $-CH_2COOMe$, Bn, PMB (MPM), 3, 4-ClBn, or R_9 is  or  .

55. **(New)** The composition of claim 53, where R_9 is $-NR_{12}R_{13}$, wherein R_{12} is methyl, ethyl, propyl, isopropyl, or butyl, optionally substituted with one or more occurrences of hydroxyl or protected hydroxyl, and R_{13} is hydrogen or lower alkyl, or $NR_{12}R_{13}$ together represents a 5- or 6-membered heterocyclic moiety.

56. **(New)** The composition of claim 53, where R_9 is $-O(CH_2)_pX_2R_{14}$, wherein X_2R_{14} together represent N_3, NMe_2, NHAc, $NHSO_2Me$, NHCONHMe, NHCONHPh, morpholine, imidazole, aminopyridine, or any one of:



57. **(New)** The composition of claim 2, where R_8 and R_9, taken together, form a saturated or unsaturated cyclic ring containing 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen.

58. **(New)** The composition of claim 2, where R_{10} is hydroxyl.

59. **(New)** The composition of claim 2, where R_{11} is hydrogen.

60. **(New)** The composition of claim 2, where Y and Z together are cyclopropyl.

61. **(New)** The composition of claim 2, where Y and Z together are –NHC(=O)-.